Cardioversion and Digitalis

II. Clinical Studies

By Robert Kleiger, M.D., and Bernard Lown, M.D.

CARDIOVERSION has proved an effective and safe method for reverting ectopic arrhythmias to sinus rhythm. However, there is increasing evidence that capacitor electrical discharge may provoke arrhythmias in experimental animals as well as in man. The majority of abnormal rhythms immediately following cardioversion are atrial in origin and are not serious. They generally represent one of three mechanisms: (1) a delayed "warm-up" of the sinus node manifested by sinus bradycardia, nodal rhythm, or escape beats, (2) increased atrial automaticity as demonstrated by individual or multiple atrial premature beats occurring either singly or in paroxysms of tachycardia, and (3) a defect in elaboration or conduction of the sinus impulse characterized by chaotic atrial activity with changing P wave contour and bradycardia interspersed with multiple and recurring ectopic beats with runs of atrial or nodal tachycardia. The first two mechanisms are transient and generally result in stable sinus rhythm within 1 to 5 minutes. The third mechanism almost invariably reverts to atrial flutter or fibrillation.

The ventricular arrhythmias following cardioversion are less common but may be more serious. These are of two types: The first occurs immediately after the shock and involves development of ventricular fibrillation usually the result of improper synchronization. The second occurs after a delay of several or more normal beats and may range from unifocal, infrequently recurring ventricular premature beats to more prolonged arrhythmia. The latter can consist of ventricular bigeminy, salvos of multifocal beats, ventricular tachycardia, or even ventricular fibrillation at times ending in death.

Patients receiving large doses of digitalis or those on maintenance digitalis therapy who have had substantial diuresis immediately prior to cardioversion are likely to show post-reversion ventricular arrhythmias. Experimental studies have demonstrated that digitalization lowers the threshold to electrical shock. In control dogs the median trans-thoracic discharge energy to produce ventricular tachycardia was 400 watt-seconds (ws). In these same animals, shortly after recovery from digitalis toxicity, 0.2 ws produced ventricular tachycardia. This represents a 2,000-fold reduction in threshold. While the experimental data indicate that condenser electrical discharge may provoke arrhythmias in the overdigitalized animal, the evidence in man is at best circumstantial and is based on but few observations. The purpose of the present study was to determine whether patients with atrial fibrillation who develop post-cardioversion ventricular arrhythmias exhibit evidence of digitalis overdosage prior to electrical treatment.

Methods

The occurrence of ventricular ectopic arrhythmias following electrical shock was studied in 107 consecutive cardioversion procedures in 100 patients with atrial fibrillation. Eighteen patients showed frequent ventricular ectopic beats, ventricular bigeminy, or ventricular tachycardia. These patients were designated as group A. The remaining 89 procedures in 82 patients (group B) resulted in either no ventricular arrhythmias or only sporadic ventricular premature beats, that is, less than 5 per minute and not persisting for more than 10 minutes.
The electrocardiograms made prior to cardioversion on the 100 patients were analyzed for abnormalities suggestive of overdigitalization. This was done without knowledge of the response to cardioversion. Arrhythmias considered as possibly due to digitalis included nodal escape, nodal rhythm, Wenckebach A-V conduction, and ventricular premature beats. In the absence of change in ventricular complex, these mechanisms may have arisen not in the A-V node but in the common bundle of His. Since such distinction has little clinical significance the term "nodal rhythm" is employed. The following definitions were adhered to:

Nodal escape—beats with unaltered QRS complexes and cycle lengths greater than 1.4 seconds.

Nodal rhythms—six or more consecutive beats with identical cycle lengths (± 0.02 seconds).

Wenckebach conduction—three or more consecutive beats showing progressive shortening of interval followed by a beat with a cycle length approximately twice the short cycle.

Patients of groups A and B were compared as to etiology of heart disease, ventricular rate while in atrial fibrillation, presence or absence of digitalis therapy, type and dose of cardiac glycosides employed, and serum potassium concentrations at the time of reversion.

Results

Group A consisted of 18 patients who developed ventricular arrhythmias immediately after cardioversion, while group B consisted of 82 patients who were free of such disorders. The following ectopic mechanisms were observed: frequent multiform ventricular extrasystoles in 15, ventricular bigeminy in 14, and ventricular tachycardia in six patients. The total exceeds 18 since a number of group A patients manifested more than one arrhythmia. The inception of ventricular arrhythmia occurred usually 2 to 5 seconds after the shock. In one patient ventricular tachycardia began 1 minute after reversion to sinus rhythm. In three patients ventricular ectopic beats persisted for more than 30 minutes; in one patient it lasted for as long as 24 hours. Of the six episodes of ventricular tachycardia, four consisted of one or more paroxysms of three consecutive ectopic beats. Two of the episodes lasted longer, one ended spontaneously after 15 seconds and one was terminated after a single 300 ws discharge. None of the patients developed ventricular fibrillation or experienced delayed untoward effects from the arrhythmia. Thirteen of the 18 (72%) in group A were reverted to sinus rhythm as compared with 82 of 89 (92%) in group B.

The appearance of serious ventricular ectopic mechanisms following electrical shock was correlated with the presence of certain arrhythmias in the precardioversion electrocardiogram. Abnormalities of rhythm in the precardioversion electrocardiogram suggestive of digitalis overdose were noted in 17 of the 18 patients in group A as compared to 41 of the 89 in group B (table 1). When the two groups are compared as to the incidence of beats with abnormal QRS complexes there were 54% in group A and 34% in group B (table 1). An altered QRS complex may represent a ventricular ectopic beat or an aberrantly conducted beat. The former but not the latter generally results from digitalis intoxication. It is not always possible to distinguish between these two types of abnormal ventricular complexes (fig. 1). A more precise conception of the incidence of digitalis in-

**Table 1**

<table>
<thead>
<tr>
<th>Incidence of Precardioversion Arrhythmias Suggestive of Digitalis Toxicity in Patients with (Group A) and Patients without (Group B) Post-reversion Ventricular Ectopic Mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>A</td>
</tr>
<tr>
<td>B</td>
</tr>
</tbody>
</table>

* Nodal escape beats, nodal rhythm and Wenckebach type of A-V conduction.
† Ectopic and aberrant conducted beats.

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Figure 1

The top strip taken prior to cardioversion shows an abnormal beat with features suggesting aberrant ventricular conduction. Within 30 seconds after reversion to sinus rhythm (NSR), however, a beat with identical morphology recurs and is now clearly identifiable as a ventricular extrasystole.

toxication is obtained from an analysis of the incidence of nodal rhythm. Nodal mechanisms prior to cardioversion were nearly three times as frequent in group A as in group B (table 1). The incidence in group A of nodal escapes and the Wenckebach type of A-V conduction was two times and that of nodal rhythm four times that seen in group B (table 2). Although the rates prior to cardioversion were similar in the two groups, the percentage of heart rates of 70 or less was three times greater in group A than in B. It may be concluded that the patient with atrial fibrillation has nearly a 50% chance of developing serious ventricular arrhythmias following cardioversion, if the heart rate is less than 70 or there are nodal escape beats, nodal rhythm, or Wenckebach type of A-V conduction (figs. 2 and 3).

Additional support for the role of digitalis in predisposing to postcardioversion arrhythmias is provided by the following observations. Six of the 18 group A patients and none of the 82 group B patients had well confirmed manifestations of digitalis intoxication, either shortly before or after cardioversion. The

| Table 2  |
| --- | --- | --- | --- | --- | --- |
| Comparison of Precardioversion Mechanisms in Group A and B Patients with Respect to the Action of Digitalis on A-V Node |
| Group | Cardioversions (no.) | Rate, 70 or more | Nodal escape (%) | Nodal rhythm (%) | Wenckebach A-V conduction (%) |
| A | 18 | 27.0 | 27.0 | 27.0 | 22.0 |
| B | 89 | 9.0 | 13.0 | 6.7 | 0.0 |
diagnosis of overdigitalization was not judged by the occurrence of arrhythmias immediately after electrical reversion. It was based on typical electrocardiographic and subjective manifestations of digitalis overdosage which abated when digitalis drugs were discontinued. The presence of heart block was also instructive. While the mean P-R interval was of the same duration in the two groups, first degree heart block was noted in 54% of group A and 37% of group B. In one patient of group A cardioversions were accomplished on two occasions.

**Figure 2**

While in atrial fibrillation (AF) the electrocardiogram reveals nodal rhythm at two fixed cycle intervals. Immediately after resorting sinus rhythm (NSR), numerous multiform and bigeminal ventricular ectopic beats occur.

**Figure 3**

Electrocardiogram of a 19-year-old, 6-month pregnant woman with severe mitral incompetence. Ventricular acceleration from 150 to 175 and regularization of response resulted after 1.75 mg of digoxin was administered intravenously over 12 hours. Cardioversion discharge at 50 ws provoked ventricular bigeminy and nodal escape beats.
different occasions. During the time of the initial reversion this patient was receiving 0.2 g of digitalis leaf daily. Within 1 minute after the electrical discharge, frequent and multiform ventricular beats developed and lasted for 30 seconds (fig. 4). Use of digitalis leaf was stopped for the ensuing 5 days at which time atrial fibrillation recurred. A second cardioversion, at the same energy as during the first reversion, restored sinus rhythm but without the occurrence of ectopic beats.

In 10 patients of group A immediately following the electrical shock, atrial arrhythmias suggestive of overdigitalization developed in addition to the ventricular ectopic beats. Two had transient episodes of paroxysmal atrial tachycardia with block (fig. 5), a disorder which when associated with multiform ventricular esctopic beats almost invariably denotes digitalis intoxication. In seven of the remaining eight there was nodal rhythm with A-V dissociation while the eighth patient showed a changing sinus pacemaker. Thus a majority of group A patients had other findings suggestive of digitalis intoxication in addition to postreversion ventricular ectopic beats. This was not the case with group B patients.

The two groups did not differ with respect to age or sex (table 3). In both groups rheumatic heart disease was the most frequent cardiac condition; there was, however, a higher incidence of patients with coronary artery disease in group A. Digitalis drugs had been administered before cardioversion to 17 of the 18 patients in group A and to 76 of the 82 patients in group B. Both groups had the same percentage of patients receiving long acting digitalis preparations. However, a greater number of patients in group A compared to those in group B were receiving digoxin in a dose of 0.5 mg daily or more. The average serum potassium concentration was the same in the two groups.

Table 3
Comparison of Patients in Group A and Group B

<table>
<thead>
<tr>
<th></th>
<th>Group A (%)</th>
<th>Group B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>39</td>
<td>41</td>
</tr>
<tr>
<td>Age</td>
<td>55 yr</td>
<td>53 yr</td>
</tr>
<tr>
<td>Rheumatic heart disease</td>
<td>61</td>
<td>68</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>Digitalis drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digitoxin or leaf</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td>Digoxin 0.5 mg/d more</td>
<td>39</td>
<td>24</td>
</tr>
<tr>
<td>Digoxin 0.25 mg/d or less</td>
<td>22</td>
<td>34</td>
</tr>
</tbody>
</table>

Figure 4
Patient was receiving 0.2 g digitalis leaf daily, rhythmic atrial fibrillation with occasional ventricular regularization (strip 1). Cardioversion restored sinus rhythm (strip 2). However, within 1 minute, ventricular multiform bigeminy developed (strip 3). Repeat reversion for recurrent atrial fibrillation after 5 days without digitalis resulted in no ectopic beats.
Thirteen of the 18 patients in group A received more than one shock. The severity of the ventricular arrhythmia in these patients increased with increase in energy of discharge (fig. 6). This was observed in 12 of 13 patients. At shocks of 50 ws only one of the 13 had bigeminy, at 100 ws six showed this response. In view of this finding the energy for reversion of group A and B was compared. The energy for group A was 120 ws and for group B 110 ws. This difference is not statistically significant.

Discussion

This analysis of 100 consecutive patients with atrial fibrillation associates the development of post-cardioversion ventricular ectopic mechanisms with the occurrence of arrhythmias prior to the electrical treatment suggestive of digitalis excess. Indeed, the patient in atrial fibrillation who exhibits paroxysms of nodal rhythm, nodal escape beats, Wenkebach type of A-V conduction, or bradycardia, has a 50% chance of developing ventricular arrhythmias following cardioversion. This is true whether or not sinus rhythm is restored by cardioversion.

A number of reports have called attention to the occurrence of serious disorders of rhythm in patients who were subjected to cardioversion while overdigitalized. Rabbino and associates have reported on three patients with arrhythmias presumably due to digitalis overdosage in whom attempted cardioversion produced ectopic ventricular activity followed by ventricular fibrillation.

Figure 5

(Upper strips). A 100 ws cardioversion discharge results in sinus rhythm for 36 seconds which is paroxysmal atrial tachycardia with variable block (PAT with block) and ventricular bigeminy.

(Lower strips). The PAT with block terminated within 2 minutes after cardioversion while the ventricular ectopic beats persisted for an additional minute.
In patients with long-standing atrial fibrillation, successive shocks at progressively higher energies result in increased incidence of multiform ventricular ectopic beats.

All three patients had received excessive doses of digitalis, two exhibited paroxysmal atrial tachycardia with block, and one had ventricular tachycardia. High initial energies were employed for these cardioversions. This result emphasizes the extreme hazard of treating digitalis toxic arrhythmias with electrical discharge. Graff and Etkins\textsuperscript{21} reported the development of ventricular tachycardia following a cardioversion discharge of 80 ws in a patient with atrial fibrillation and mitral insufficiency. The patient was on a daily maintenance dose of digoxin of 0.75 mg which had been stopped for 2 days prior to the reversion. A very short strip of electrocardiogram, used by the authors to illustrate the rhythm prior to cardioversion, demonstrated regularization of the ventricular response and suggested that the patient may have been overdigitalized.

In other reports of arrhythmias following cardioversion, the possible role of digitalis was not defined.\textsuperscript{2, 6, 15, 22, 23} Gilbert and Cuddy\textsuperscript{17} reported recently on post-cardioversion arrhythmias as they relate to the state of digitalization. This report is based on 44 patients who were subjected to cardioversion. The presence of digitalis intoxication in the majority of these patients was judged by the occurrence of first degree A-V block. However it has been shown that prolonged A-V conduction is an attribute of the patient with chronic atrial fibrillation.\textsuperscript{24} Gilbert and Cuddy\textsuperscript{17} stated that the arrhythmias following cardioversion are due to the restoration of sinus rhythm rather than to the administered electrical shock. They offered no explanation as to why sinus rhythm should predispose to digitalis intoxication. They maintained that similar arrhythmias occur when quinidine is employed for reversion. If A-V block is used as the major criterion for judging digitalis toxicity, it would follow that a high incidence of “toxicity” would be encountered whatever the method of reversion. This would occur because, as already stated, patients who

\textsuperscript{Circulation, Volume XXXIII, June 1966}
develop atrial fibrillation have impaired A-V conduction. Two lines of evidence support the view that the electrical discharge rather than the redevelopment of sinus rhythm is the critical factor. In the first place these arrhythmias follow electrical shock when sinus mechanism is not restored; in the second place a direct correlation exists between the energy of discharge and the development of digitalis-like arrhythmias. Recent animal experiments have provided decisive evidence that digitalization to a near-toxic endpoint strikingly lowers the threshold for electrical discharge.18

The mechanism by which electrical discharge provokes digitalis arrhythmias in the marginally or fully overdigitalized patient remains to be defined. Several hypotheses have been presented.18 The most likely is that the electrical discharge affects myocardial cellular membranes resulting in a loss of intracellular potassium. The leakage of ion may continue for seconds or even minutes after the discharge. When a critical loss has occurred, toxic effects from myocardial bound glycoside ensue. The reaction does not occur instantaneously with the shock since both in animals and man there may be a delay before arrhythmia develops. In support of this hypothesis is the experimental observation that administration of potassium prevents postshock arrhythmias, while an infusion of glucose and insulin, which lowers the concentration of extracellular potassium, markedly potentiates and prolongs this phenomenon.25

In the light of these findings, we have followed certain practices which have greatly reduced the risk attending cardioversion of the digitalized patient. Overt digitalis toxic arrhythmias are treated with drugs and not with cardioversion. In the experimental animal such arrhythmias have proved resistant to electrical discharge.18, 26 In patients with digitalis induced arrhythmias electrical treatment is fraught with the danger of inducing irreversible ventricular tachycardia and death.16, 17 In elective reversions, if the patient is receiving digoxin, it is discontinued for 24 hours. If a longer-acting digitalis drug is employed, its use is stopped for 2 days. Gilbert and Cuddy17 have suggested that cardiac glycosides be withheld for 5 days to 10 days. Such a practice is unnecessary and not without danger. When the patient is deprived of digitalis drugs, congestive heart failure may redevelop and atrial fibrillation may recur promptly as a result. Furthermore, in the undigitalized patient the heart rate may accelerate to high levels once quinidine therapy is instituted prior to cardioversion. If the patient has a limited cardiac reserve, decompensation may occur. Indeed, such a complication is reported by Gilbert and Cuddy.17

Whenever the precardioversion electrocardiogram shows abnormalities suggestive of digitalis overdose, elective reversion is postponed. Digitalis is stopped until the arrhythmia clears. Cardioversion is similarly delayed in the presence of hypokalemia until the electrolyte derangement is corrected. Diuretics are withheld for 1 to 2 days before reversion. It has been our experience that the overdigitalized patient with atrial fibrillation is more difficult to revert and may require more energy to restore sinus rhythm. Thus, in the present study only 72% of the patients showing post-cardioversion arrhythmia were reverted as compared to 92% of the control groups. The occurrence of post-cardioversion arrhythmia is directly related to the energy of discharge. Our practice is, therefore, to start with 25 to 50 ws. If reversion is not achieved, the energy is then increased to 100 ws and thereafter is raised by 100 ws increments until sinus rhythm is restored or a discharge of 400 ws had been given. Such a method of employing the least energy needed for reversion diminishes the possibility of producing serious arrhythmias. If ventricular ectopic beats occur after the first shock and increase in frequency with the next higher discharge, one has the option of either discontinuing the procedure or of administering antiarrhythmic drugs before proceeding with still higher energies. The serious complications in digitalized patients reported to date have occurred after initial shocks of 200 to
Such high energies are excessive for restoring sinus rhythm in the majority of patients with atrial fibrillation. Thus in 200 consecutive cardioversions of patients with atrial fibrillation, employing anteroposterior paddle placements, 80% were restored to sinus rhythm with energies of 100 ws or less.

In emergency situations where prompt reversion is mandatory and the patient has received large doses of digitalis, cardioversion is initiated with 25 ws. If ectopic beats develop, generally they can be abolished by the intravenous administration of one of the following drugs: lidocaine 50 mg, procaine amide 100 mg, diphenylhydantoin 100 mg, or propranolol 5 mg. These agents can be repeated as the energy of successive shocks is increased and ectopic mechanisms recur. If these measures are applied, the appreciable risk associated with cardioversion of the over-digitalized patient can be minimized.

In 650 cardioversions we have not encountered a single episode of ventricular fibrillation or cardiac standstill immediately following the procedure. Attention to proper technique is one important factor in this record of safety. Another factor is the recognition that even minor degrees of digitalis toxicity predispose to post-cardioversion arrhythmias. A group of arrhythmias which may develop within 30 minutes to many hours after the reversion remains. These are probably the result of quinidine cardiotoxicity. Selzer and Wray27 reported eight cases of quinidine syncope caused by transient bouts of ventricular fibrillation. In two of these cases the syncope followed cardioversion, in one after 30 minutes and in the second after 24 hours. They estimated that 3 to 4% of patients receiving quinidine may develop these arrhythmias. Castelanos and associates28 have also reported four cases of quinidine syncope due to ventricular fibrillation following cardioversion. These authors feel that capacitor shock may unmask or make worse latent quinidine intoxication. In three of these four cases precadioversion tracings already suggested the presence of quinidine toxicity. Thus, the major hazard of cardioversion relates to the use of drugs: digitalis being implicated in the immediate arrhythmias and quinidine being responsible for the delayed rhythm disorders.

Summary

The electrocardiograms before and immediately after cardioversion of 100 consecutive patients with chronic atrial fibrillation treated at the Peter Bent Brigham Hospital have been analyzed. Evidence of digitalis intoxication in the precardioversion tracing was associated with a significant increase in the incidence of serious ventricular ectopic activity following electrical shock. The role of digitalis in post-cardioversion arrhythmias is reviewed. The measures to reduce the incidence and gravity of such arrhythmias are outlined.

References

Successful Search for Authorship

Thus in this pursuit of source material I discovered Mrs. Sarah Hoare, a minor British poet of the early 19th century, whose poems devoted to flowers, included this much-quoted verse dedicated to the foxglove:

And Digitalis wisely given,
Another boon of favoring Heaven
Will happily display;
The rapid pulse it can abate,
The hectic flush can moderate,
And blast by him, whose will is fate,
May give a happier day.

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